

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/EP2004/012384

International filing date (day/month/year)
02.11.2004

Priority date (day/month/year)
03.11.2003

International Patent Classification (IPC) or both national classification and IPC
A61K9/50, C12N5/08

Applicant
UNIVERSITA' DEGLI STUDI DI MILANO

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2004/012384

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
☐ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material:
☐ in written format
☐ in computer readable form
 - c. time of filing/furnishing:
☐ contained in the international application as filed.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2004/012384

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:
- ☐ paid additional fees.
 - ☐ paid additional fees under protest.
 - ☒ not paid additional fees.
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with
 - ☒ not complied with for the following reasons:
see separate sheet
4. Consequently, this report has been established in respect of the following parts of the international application:
- ☐ all parts.
 - ☒ the parts relating to claims Nos. 1-50 in part

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-50
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-50
Industrial applicability (IA)	Yes: Claims	1-50
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Reference is made to the following documents:

- D1: PANGAS STEPHANIE A ET AL: Novel approach for the three-dimensional culture of granulosa cell-oocyte complexes. TISSUE ENGINEERING, vol. 9, no. 5, October 2003, pages 1013-1021.
- D2: EP-A-0 922 451 (UNIVERSITA DI PAVIA; UNIVERSITA' DEGLI STUDI DI MILANO; UNIVERSITA' DE) 16 June 1999.

The present application concerns alginate microencapsulation of ovarian cells, stem cells, gametes, and mammalian embryos. The method disclosed results in capsules comprising an outer alginate membrane and a core of cells and an artificial extracellular matrix.

Re Item IV

Lack of unity of invention

1. Rule 13, PCT Lack of unity of invention

The IPEA agrees with the objection put forward by the ISA as to lack of unity; the arguments presented in the annex to the non-unity objection are fully maintained. No further search fee has been paid within the allocated time [Rule 40(3) PCT]. The International Preliminary Examination will therefore be limited to what appears to be the main invention i.e. the searched part of the application [see the non-unity objection dated 07.04.2005; see also Rule 66(1)(e) PCT and PCT Preliminary Examination Guidelines C-III 7.8 - 7.10; C-VI 5.1a].

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Novelty, Art.33(1) and (2), PCT

Subject-matter referred to in claims 1-50 in part concerning encapsulation of ovarian cells (invention 1) resulting in an outer alginate membrane and a core of ovarian cells and an artificial extracellular matrix has not been disclosed in the prior art and appears to be novel under Art.33 (2), PCT.

2. Inventive Step, Art.33(1) and (3), PCT

Invention 1 of the present application concerns alginate microencapsulation of ovarian cells resulting in capsules comprising an outer alginate membrane and a core of ovarian cells and an artificial extracellular matrix. In D1, which may be considered the closest prior art, microencapsulation of ovarian cells by extrusion of an alginate/cell

mixture into a salt solution is disclosed. From this subject-matter of the present application differs in that a salt/ECM/cell mixture is extruded into an alginate solution resulting in a liquid core and an outer alginate membrane. The technical problem thus appears to be the provision of an alternative encapsulation of ovarian cells. The choice of salt/ECM/cell extrusion into an alginate solution appears to be obvious in the light of D2 which discloses said method for sperm cells. Thus the solution to the technical problem put forward by the present application appears to be not more than a combination of technical features known from D1 and D2, without the provision of any surprising effects and obvious to the skilled person in the art. Therefore subject-matter referred to in claims 1-50 as far as they refer to invention 1 does not appear to involve an inventive step under Art. 33 (3), PCT.

3. Industrial Applicability, Art.33 (1) and (4), PCT

Subject-matter of invention 1 of the present application appears to be industrially applicable under Art.33(1) and (4), PCT.

Re Item VIII

Certain observations on the international application

1. Clarity of Claims and Support by the Description, Art.6, PCT

The term instrumentation used in independent claim 19 and referred to in dependent claims 20-26 is vague and unclear and leaves the reader in doubt as to the meaning of the technical features to which it refers, thereby rendering the definition of the subject-matter of said claims 19-26 unclear, Article 6 PCT.

2. Exceptions to patentability

It is pointed out to the applicant that upon entry into the regional phase subject-matter claimed in the present application might not be patentable. The EPO, for example, does not recognize as patentable subject-matter relating to the use of human ovarian follicular cells for commercial purposes. Such claims are considered to be covered by the exclusion clause of Rule 23e(1) EPC, which states that the human body at the various stages of its development, including germ cells (see C-IV, 3.3b of the Guidelines for the Examination in the EPO), cannot constitute a patentable invention.

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